MaineCare Services
An Office of the Department of Health and Human Services
Paul R. LePage, Governor Mary C. Mayhew, Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 6/29/2017
RE: Maine DUR Board **Meeting** minutes from June 27, 2017

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD	X		
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR	X		
Mike Antoniello, MD			X
Kathleen Polonchek, MD			X
Kenneth McCall, PharmD	X		
Steve Diaz, MD	X		
Erin Ackley, PharmD.	X		
Corinn Martineau, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jeffrey S. Barkin MD, DFAPA Change Healthcare	X		
Jan Wright, Pharmacy Supervisor, OMS	X		X
Christopher Pezzullo, State Health Officer DHHS, DO	X		
Jill Kingsbury, MaineCare Pharmacy Director	X		

Guests of the Board:

CALL TO ORDER: 5:30PM

Dr. Pezzullo called the meeting to order at 5:30 PM.

PUBLIC COMMENTS

Paul Isikwe from Sanofi Genzyme: Highlighted the attributes of Dupixent.
Syed Mahmod from PYC Therapeutic: Highlighted the attributes of Emflaza.
Michael Callahan from Genentech: Highlighted the attributes of Ocrevus.
Amy Tomasello and Steven Birch from Sunovion: Highlighted the attributes of Utibron.
Tyson Park from Teva: Highlighted the attributes of Austedo.
Thiken Padukkavidara from Takeda: Highlighted the attributes of Alunbrig.
Thom Board from Neurocrine: Highlighted the attributes of Ingrezza.

OLD BUSINESS

DUR MINUTES

The June DUR meeting minutes were accepted as written.

MAINECARE UPDATE

No update at this time.

ELIDEL AND PROTOPIC PREFERED

Last meeting conversation during closed session discussed moving Elidel and Protopic to preferred but was not voted on during open session. Motion was made to make Elidel and Protopic preferred.

Board Decision: The Board unanimously approved the above motion.

RETRO-DUR ADDITIONAL DATA ON CO-PRESCRIBING OF STIMULANTS, BENZODIAZEPINES AND Z DRUGS

Stimulants have been shown to markedly improve the symptoms of ADD and ADHD. Many people with these disorders also experience anxiety requiring treatment, either behavioral psychotherapy, pharmacologic treatment, or both. In addition, sleep disorders are relatively common in this group. While SSRIs and SNRIs are recommended to address anxiety in these patients, benzodiazepines can be used to treat acute episodes while waiting for SSRIs or SNRIs to demonstrate efficacy as it take up to 12 weeks to achieve effectiveness.

In the general population, so called "Z" drugs (zolpidem, zaleplon, and zopiclone), are widely prescribed for sleep disorders, most commonly chronic insomnia. Sleep disorders are common among patients with numerous psychiatric diagnoses including mood disorders, anxiety disorders, attentional disorders, and autism. Generally, stimulants, benzodiazepines and Z drugs should not be used in combination due to overlapping CNS effects, including worsening anxiety and mood, confusion, lethargy, obtundation, bradycardia, respiratory depression, agitation and aggressive behavior. In children, the recommendation is to treat anxiety and sleep disorders initially with behavioral therapy, followed by antidepressants (SSRIs), if needed. Benzodiazepines and Z drugs are not recommended for children.

Identify members with diagnoses of ADD, ADHD, and ASD, stratified by age, and identify use of stimulants, "Z" drugs, and benzodiazepines concomitantly for greater than a 30day period of overlap. Age stratification will be age bands 0-10, 11-20, 21-30 and 31 and over. Additionally, data may identify prescribers to evaluate whether there is a need for an education program around the use of these drugs generally, or if there are a limited number of prescribers not following guidelines.

Additional data requested:
Add opiates (GPI65) to analyst
Compile the list of prescribers including location (county) and list number of patients in descending order.

Recommendation: Leave up to the board if after reviewing the additional results: 1. no further action is required at this time; or 2: Perform an outreach either by phone or letter to the top prescribers.

Board Decision: OMS will draft a personalized letter to the top 20 prescribers and decided who as a contact person will be put on the letter either Dr. Pezzullo, DUR rep or CHC rep.

NEW BUSINESS

RETRO-DUR DATA PRESENTATION: ASSESSING THE PATTERN OF USAGE OF LONG-ACTING STIMULANTS, SPECIFICALLY LOOKING AT MONTH THAN ONCE A DAY DOSING PATTERNS AND USE AMONG DIFFERENT AGE DRUGS, INCLUDING PEDIATRICS.

Defer presentation to another meeting. Clarify data pull to look at in patients on Stimulants how many psych medications are they on separated into age bans.

INTRODUCE: CO-PRESCRIBING OF OPIATE PAIN MEDICATIONS (INCLUDING COUGH SYRUPS), BENZODIAZEPINES AND "Z" DRUGS

The increased use and misuse of opioid pain medications and benzodiazepines is well documented and use of hypnotics (specifically "Z" drugs) for sleep is widespread. Polypharmacy with these drugs is not uncommon and there is increasing recognition of severe adverse effects when these drugs are combined, especially in those who take high doses of opioids on a daily basis. Accumulating data shows that there is a high degree of sleep disordered breathing in patients on chronic opioids. While the exact mechanism is not completely understood, the effects seem to be primarily due to central sleep apneas. Recent meta-analysis showed the overall incidence of sleep disordered breathing to range from 42-85%. Risk factors are thought to be advancing age, obesity or low BMI, male sex, a daily dose of opioid greater than 200 morphine equivalents and the use of benzodiazepines.

"Z" drugs and benzodiazepines have a similar risk of respiratory depression. "Z" drugs, like benzodiazepines, enhance the activity of the inhibitory neurotransmitter gamma aminobutyric acid (GABA) via selective agonism at the benzodiazepine-1 receptor. This activation causes inhibition of neural action potentials and decreases neuronal excitability. The FDA posted a Safety Alert in August, 2016 warning of the increased risk of adverse effects, including respiratory depression and death in those using opioids combined with other CNS depressants. The FDA since then has required Black Box Warnings of these risks in the prescribing information of opioids (including cough medicines) and benzodiazepines.

Recommendation: We propose to look at the number of MaineCare members who are taking both opioids and at least one other CNS depressant in the form of a benzodiazepine or Z drug, or both. We will use paid, non-reversed Medicaid pharmacy and medical claims data from CY2016. Will identify members on opioids for greater than 30 days and divide them into those taking more or less than 200 mg morphine equivalents. Will then identify which of these members are on benzodiazepines or Z drugs (or both), not limiting our search to those who are on these medications chronically. We will examine medical claims of these members to evaluate if medical care was required due to adverse effects from any combination of these drugs. Specifically, we will highlight ED visits and admissions, with particular attention to falls, overdoses and fractures.

AirDuo® RespiClick (fluticasone propionate & salmeterol); **PDL category**- Antiasthmatic- Adrenergic Combinations

AirDuo® Respiclick is a dry powder for oral inhalation combination product containing fluticasone (a synthetic corticosteroid, with anti-inflammatory activity) and salmeterol (a long-acting beta-2 adrenergic agonist [LABA], causing relaxation of bronchial smooth muscle). It is indicated for the treatment of asthma in patients aged 12 years and older. It is not indicated for the relief of acute bronchospasm. Administer one oral inhalation BID. It is recommended to rinse the mouth with water without swallowing after each dose. The starting dose is per patient's asthma severity, with the usual recommended starting dose if not on inhaled corticosteroids being 55/14mcg BID. If switching from another inhaled corticosteroid or combination product, select the dose strength of AirDuo® Respiclick of low (55/14mcg), medium (113/14mcg) or high (232/14mcg) based on the strength of the previous inhaled corticosteroid product or the strength of the inhaled corticosteroid from a combination product and disease severity. Trials 1 and Trial 2 were conducted with adults and adolescent patients (N=1375) with baseline FEV1 40% to 85% of predicted normal with asthma not optimally controlled on current therapy. Trial 1 was a 12-week study that compared fluticasone propionate multidose dry powder inhaler 55mcg and 113mcg with AirDuo® Respiclick 55/14mcg and 113/14mcg and placebo in adults with persistent symptomatic asthma despite low-dose or mid-dose inhaled corticosteroid (ICS) or ICS/LABA therapy. Results suggested that both doses of AirDuo® Respiclick (55/14mcg least square mean change of 0.319L and 113/14mcg least square mean change of 0.315L) had significantly greater improvements in trough FEV1 as compared with Armonair® 55mcg, Armonair® 113mcg and placebo.

Recommendation: AirDuo ® be non-preferred.

Clinical Criteria: For patients ≥ 12 years and older. AirDuo® Respiclick be non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications. DDI: Avoid concomitant use of strong CYP3A4 inhibitors (e.g. ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ketoconazole, telithromycin) with AirDuo® Respiclick is not recommended due to increased systemic corticosteroid and increased cardiovascular adverse effects.

Alunbrig ® (brigatinib); **PDL category**- Cancer

Brigatinib, the active ingredient of Alunbrig®, is a tyrosine kinase inhibitor with in vitro activity at clinically achievable levels against multiple kinases, including ALK, ROS1, insulin-like growth factor-1 receptor (IGF-1R), and FLT-3 as well as EGFR deletion and point mutations, among st others. Brigatinib also reduced tumor burden and prolonged survival in animal studies. It is indicated for the treatment of anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Recommended dosage is take 90mg PO QD for the first 7 days; if 90mg is tolerated, then increase to 180mg PO QD and continue until disease progression or

unacceptable toxicity. Concomitant use with itraconazole, a strong CYP3A4 inhibitor, increased brigatinib levels. It is recommended to avoid the concomitant use of strong CYP3A inhibitors with Alunbrig®.

Recommendation: Alunbrig ® be non-preferred

Clinical Criteria: PA required to confirm appropriate diagnosis and testing. DDI: Avoid the concomitant use of strong CYP3A inhibitors with Alunbrig®, including but not limited to certain antivirals (e.g. boceprevir, cobicistat, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir), macrolide antibiotics (e.g. clarithromycin), antifungals (e.g. itraconazole, ketoconazole, posaconazole, voriconazole), and conivaptan. In addition, avoid grapefruit or grapefruit juice.

Arymo ® ER (morphine sulfate, extended-release); **PDL category**- Narcotics, Long-Acting

Morphine sulfate, the active ingredient of Arymo® ER, is a full opioid agonist and is relatively selective for the mu-opioid receptor; however, it can bind to other opioid receptors at higher doses. Like all full opioid agonists, there is no ceiling effect for analgesia with morphine. While the exact mechanism of the analgesic action is not known, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug. Indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Recommendation: Arymo® ER be non-preferred.

Austedo ® (deutetrabenazine); **PDL category**- Movement Disorders
Deutetrabenazine, the active ingredient of Austedo®, is a vesicular monamine transporter 2 (VMAT2) inhibitor. Its exact mechanism of action for its anti-chorea effects is not known, but it is thought to be related to its effect as a reversible depleter of monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals. The major metabolites of deutetrabenazine are reversible inhibitors of VMAT2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores. It is indicated for the treatment of chorea associated with Huntington's disease. Providers should periodically re-evaluate the need for Austedo® by assessing the effect on chorea and possible adverse events. In some patients, the underlying chorea itself may improve over time, thus decreasing the need for Austedo®. Austedo® has a box warning regarding the increased risk of depression and suicidal thoughts and behaviors (suicidality) in patients with Huntington's disease. If considering the use of Austedo®, the risk of depression and suicidality must be balanced with the clinical need for treatment of chorea. It is recommended to closely monitor patients for the emergence or worsening of depression, suicidality or unusual changes in behavior. Extreme caution should be used in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in Huntington's disease. The safety and efficacy of Austedo® were established mainly in study 1, a randomized, double-blind, placebo-controlled study that included ambulatory patients (N=90) with manifest chorea associated with Huntington's disease.

Recommendation: Austedo ® be non-preferred in a new category Movement Disorders.

Clinical Criteria: Clinical PA required for appropriate diagnosis.

Bavencio ® (avelumab); **PDL category**- Cancer

Avelumab, the active ingredient of Bavencio®, is a programmed death ligand-1 (PD-L1) blocking antibody, a human IgG1 lambda monoclonal antibody. PD-L1 may be expressed on tumor cells and tumor-infiltrating immune cells. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation, and cytokine production. Avelumab binds PD-L1 and blocks the interaction between PD-L1 and its receptors PD-1 and B7.1. This interaction releases the inhibitory effects of PD-L1 on the immune response resulting in the restoration of immune responses, including anti-tumor immune responses. In animal models, blocking PD-L1 activity resulted in decreased tumor growth. It is indicated for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Recommendation: Bavencio ® be non-preferred.

Clinical Criteria: PA required to confirm appropriate diagnosis and testing. For patients ≥ 12 years of age.

Dupixent ® (dupilumab); **PDL category**- Topical- Atopic Dermatitis

Dupilumab, the active ingredient of Dupixent®, is an interleukin-4 receptor alpha antagonist produced by recombinant DNA technology in Chinese Hamster Ovary culture. It is a human monoclonal antibody of the IgG4 subclass that binds to the IL-4Rα subunit and inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling. Blocking IL-4Rα with Dupixent® inhibits IL-4 and IL-13 cytokine-induced responses, including the release of proinflammatory cytokines, chemokines, and IgE. Indicated for the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. It can be used with or without topical corticosteroids. The safety and efficacy of Dupixent® have not been established in the treatment of asthma. Patients with comorbid asthma should be advised not to adjust or stop asthma medications without consulting healthcare provider. The safety and efficacy of Dupxient® were assessed in 3 randomized, double-blind, placebo-controlled trials that included adults with moderate-to-severe atopic dermatitis (AD) not adequately controlled by topical medication(s).

Recommendation: Dupixent ® be non-preferred in new category Topical- Atopic Dermatitis**.**

Clinical Criteria: Preferred drugs also indicated for this condition, including topical steroids, cyclosporin AND calcineurin inhibitors must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists. Avoid live vaccines if treated with Dupixent.

Emflaza ® (Muscular Dystrophy Agents); **PDL category**- Muscular Dystrophy Agents

Deflazacort, the active ingredient of Emflaza®, is a corticosteroid prodrug, whose active metabolite (21-desDFZ) acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. Nevertheless, the exact mechanism of action for use in patients with Duchenne muscular dystrophy is not known. It is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of

age and older. Patients taking corticosteroids, including Emflaza®, and concomitant therapy with neuromuscular blocking drugs may be at increased risk of developing acute myopathy. There is some evidence to suggest that Emflaza® may have fewer adverse effects that lead to discontinuation than prednisone and that weight gain adverse effects are less likely to be moderate to severe compared to prednisone; however, there is no evidence at this time to support that Emflaza® is more effective than the currently available, more cost effective medications.

Recommendation: Emflaza ® be non-preferred.

Clinical Criteria: For the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older and a documented intolerance of oral corticosteroid.

Ingrezza ® (valbenazine); **PDL category**- Movement Disorders

Valbenazine, the active ingredient of Ingrezza®, is a vesicular monoamine transporter 2 (VMAT2) inhibitor. Its mechanism of action in the treatment of tardive dyskinesia is not known, but it is thought to be mediated through the reversible inhibition of VMAT2, a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle for storage and release. It is indicated for the treatment of adults with tardive dyskinesia. Avoid concomitant use of Ingrezza® with MAO inhibitors (e.g. isocarboxazid, phenelzine, or selegiline). Concomitant use with strong CYP3A4 inducers (e.g. rifampin, carbamazepine, phenytoin, St. John's wort) is not recommended. Ingrezza® is the first FDA approved medication for the condition of tardive dyskinesia, however tetrabenazine does carry an orphan drug designation for this indication.

Recommendation: Ingrezza ® be non-preferred in new PDL category Movement Disorders.

Clinical criteria: Clinical PA required for appropriate diagnosis. DDI: Avoid concomitant use of Ingrezza® with MAO inhibitors (e.g. isocarboxazid, phenelzine, or selegiline). Concomitant use with strong CYP3A4 inducers (e.g. rifampin, carbamazepine, phenytoin, St. John's wort) is not recommended.

Kisqali ® (ribociclib); **PDL category**- Cancer

Ribociclib, the active ingredient of Kisqali®, is a kinase inhibitor. It is an inhibitor of cyclin-dependent kinase (CDK) 4 and 6. These kinases are activated upon binding to D-cyclins and play an important role in signaling pathways which lead to cell cycle progression and cellular proliferation. It is indicated to use in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. There is no pregnancy category with this medication; however, the risk summary indicates that based on findings from animal studies and its mechanism of action, Kisqali® can cause fetal harm when administered to a pregnant woman. There are no available human data informing the drug-associated risk. Recommended dosage is to take 3 tablets (600mg) PO QD for 21 consecutive days with or without food followed by 7 days off treatment resulting in a complete cycle of 28 days. Coadminister with letrozole 2.5mg QD taken throughout the 28-day cycle. Both should be taken together, preferably in the morning. Use caution when Kisqali® is administered with CYP3A substrates with a narrow therapeutic index. The dose of a sensitive CYP3A substrate with a narrow therapeutic index, including but not limited to alfentanil, cyclosporine, dihydroergotamine, ergotamine, everolimus, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus, may need to be reduced as ribociclib can increase their exposure.

Recommendation: Kisqali ® be non-preferred.

Clinical Criteria: PA required to confirm appropriate diagnosis and testing. Kisqali requires prior authorization to verify diagnosis and concomitant.

Board Decision: The Board unanimously approved all the above recommendation.

Lartruvo ® (olaratumab); **PDL category**- Cancer

Olaratumab, the active ingredient of Lartruvo®, is a recombinant human IgG1 monoclonal antibody that binds specifically to human platelet-derived growth factor receptor alpha (PDGFR-α). PDGFR-α is a receptor tyrosine kinase on cells of mesenchymal origin. Signaling through this receptor plays a role in cell growth, chemotaxis, and mesenchymal stem cell differentiation. The receptor has also been found on some tumor and stromal cells, including sarcomas, where signaling can contribute to cancer cell proliferation, metastasis, and maintenance of the tumor microenvironment. The interaction of olaratumab and PDGFR-α prevents binding of the receptor by specific ligands. Indicated for use in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery. This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial. In an open-label clinical trial, Lartruvo® plus doxorubicin was found to be significantly more effective for overall survival rates as compared with doxorubicin alone.

Recommendation: Lartruvo ® be non-preferred.

Clinical Criteria: PA required to confirm appropriate diagnosis and testing.

Board Decision: The Board unanimously approved all the above recommendation.

Morphabond® ER (morphine sulfate, extended- release); **PDL category**- Narcotics, Long-Acting

Morphine sulfate, the active ingredient of Morphabond® ER, is a full opioid agonist and is relatively selective for the mu-opioid receptor; however, it can bind to other opioid receptors at higher doses. Like all full opioid agonists, there is no ceiling effect for analgesia with morphine. While the exact mechanism of analgesic action is not known, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug. Indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Morphabond® ER for use in patients for whom alternative treatment options (e.g. non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Morphabond® ER is not indicated as an as-needed (prn) analgesic. When Morphabond® ER treatment is no longer needed, taper the dose gradually, by 25-50% every 2 to 4 days. Do not abruptly discontinue treatment.

Recommendation: Morphabond® ER be non-preferred.

Board Decision: The Board unanimously approved all the above recommendation.

Ocrevus® (ocrelizumab); **PDL category**- Multiple Sclerosis- Non-Interferons

Ocrelizumab, the active ingredient of Ocrevus®, is a recombinant humanized monoclonal antibody directed against CD20-expressing B-cells. It is a glycosylated immunoglobulin G1 (IgG1). Its exact mechanism of action for use in multiple sclerosis (MS) is not known, but it is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. After cell surface binding to B lymphocytes, ocrelizumab results in antibody-dependent cellular cytolysis and complement-mediated lysis. Indicated for the treatment of adult patients with relapsing or primary progressive forms of MS. Ocrevus® was found to be significantly more effective as compared with Rebif® for reducing the annualized relapse rate (ARR) (primary endpoint) in patients with RMS, as well as for other secondary endpoints. It was found to be significantly more effective than placebo in the clinical trials with PPMS for reducing the primary endpoint of the proportion of patients with 12-week confirmed disability progression.

Recommendation: Ocrevus ® be non-preferred.

Clinical Criteria: Clinical PA is required to establish diagnosis and medical necessity.

Board Decision: The Board unanimously approved all the above recommendation.

Rhofade® (oxymetazoline); **PDL category**- Topical-Acne Preparations

Oxymetazoline, the active ingredient of Rhofade®, is an alpha1A adrenoceptor agonist that acts as a vasoconstrictor. It is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults. Use caution in patients receiving concomitant alpha-1 adrenergic receptor antagonists, such as in the treatment of cardiovascular disease, BPH, or Raynaud's disease. In addition, use caution in patients taking MAO inhibitors. Rhofade® may impact blood pressure and should be used with caution in patients with severe, unstable or uncontrolled cardiovascular disease, orthostatic hypotension, and uncontrolled hypertension or hypotension. Patients should seek immediate medical care if conditions worsen in these patient populations. In addition, Rhofade® should be used with caution in patients with cerebral or coronary insufficiency, Raynaud's phenomenon, thromboangiitis obliterans, scleroderma, or Sjogren's syndrome. The safety and efficacy of Rhofade® were assessed in 2 identical, randomized, double-blind, vehicle-controlled studies that included patients with persistent erythema associated with rosacea (N=885). Rhofade® or vehicle were used once daily for 29 days. Disease severity was graded by a clinician using a 5-point clinician erythema assessment (CEA) scale and by the subject on a similar 5-point subject self-assessment (SSA) scale. Subjects scored either moderate or severe on both scales.

Recommendation: Rhofade ® be non-preferred.

Board Decision: The Board unanimously approved all the above recommendation.

Rydapt® (midostaurin); **PDL category**- Cancer

Midostaurin, the active ingredient of Rydapt®, is a multikinase inhibitor. It is a small molecule that inhibits multiple receptor tyrosine kinases. It has been shown to inhibit FLT3 receptor signaling and cell proliferation, and it induced apoptosis in leukemic cells expressing ITD and TKD mutant FLT3 receptors or overexpressing wild type FLT3 and PDGF receptors. It has also demonstrated the ability to inhibit KIT signaling, cell proliferation, histamine release and induce apoptosis in mast cells. It is indicated to be used in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy, for the treatment of adults with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by a FDA approved test. It is not indicated as a single-agent induction therapy for the treatment of patients with AML. It is indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL). It is not indicated as a single agent induction therapy for the treatment of patients with AML. It was found to be significantly effective as compared to placebo for an increase in overall survival. It is also indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL). The safety and efficacy of Rydapt® in combination with chemotherapy were assessed in a randomized, double-blind, placebo-controlled study that included patients with newly diagnosed FLT3-mutated AML. Patients, with a median age of 47 years, were randomized to Rydapt® or placebo per protocol atFDA approved doses. Efficacy was established per overall survival (OS), measured from the date of randomization until death by any cause. The primary analysis was performed after a minimum follow-up of about 3.5 years after the randomization of the last patient. Results suggested that Rydapt® plus standard chemotherapy was superior to placebo plus standard chemotherapy.

Recommendation: Rydapt ® be non-preferred.

Clinical Criteria: Rydapt requires clinical prior authorization to verify the diagnosis, appropriate FLT-3 testing and use of recommended concurrent chemotherapy with AML diagnosis, OR the appropriate diagnosis of categories of mast cell disease.

Board Decision: The Board unanimously approved all of the above recommendation.

Spinraza® (nusinersen); **PDL category**- Neurologicals, SMA

Nusinersen, the active ingredient of Spinraza®, is a modified antisense oligonucleotide (ASO) to treat spinal muscular atrophy caused by mutations in chromosome 5q that lead to SMN protein deficiency. Per animal studies, Spinraza® was shown to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein. It is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. Prior to starting therapy, and prior to each dose, and as clinically needed, conduct the following laboratory tests: platelet count, prothrombin time, activated partial thromboplastin time, and quantitative spot urine protein testing. Spinraza® is to be administered intrathecally by, or under the direction of, healthcare professionals experienced in performing lumbar punctures. In an interim analysis, its use resulted in a statistically significantly greater percentage of patients who achieved motor milestone response as compared with a sham-control group.

Recommendation: Spinraza ® be non-preferred in a new PDL category Neurologics- SMA.

Clinical Criteria: Clinical PA is required to establish diagnosis and medical necessity. Spinraza: The diagnosis is spinal muscular atrophy (SMA) type 1, 2, or 3 (results of genetic testing must be submitted) AND The patient has at least 2 copies of the SMN2 gene AND The prescriber is a neurologist, pulmonologist, or other physician with expertise in treating SMA AND The need for invasive or noninvasive ventilation (if applicable) does not exceed more than 6 hours per 24-hour period AND Baseline motor ability has been established using one of the following exams:

Hammersmith Infant Neurological Exam (HINE)
Hammersmith Functional Motor Scale Expanded (HFMSE)
Upper Limb Module Test (non-ambulatory)

Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) AND Prior to starting therapy, and prior to each dose, the following laboratory tests will be conducted: Platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and quantitative spot urine protein

Note: Initial approval will be granted for 4 loading doses (the first 3 loading doses should be administered at 14-day intervals; the 4th loading dose should be administered 30 days after the 3rd dose). Renewal may be granted for up to 12 months with a maximum of 3 doses approved per year (12mg (5ml) every 4 months). For therapy continuation, clinical documentation must be submitted documenting improvement or maintenance of motor ability OR slower progression of disease than would otherwise be expected.

Board Decision: The Board unanimously approved all the above recommendation.

Synjardy® XR (empagliflozin & metformin extended- release); **PDL category**- Hypoglycemics, SGLT2 Inhibitor Combinations

Synjardy® XR is a combination product that contains two active ingredients with complementary mechanisms of action to aid in glycemic control. Empagliflozin is an inhibitor of sodium glucose co-transporter 2 (SGLT2); SGLT2 is the main transporter that works to reabsorb glucose from the glomerular filtrate back into the circulation. With the blocking of SGLT2, empagliflozin increases urinary glucose excretion. Metformin extended-release lowers basal and postprandial plasma glucose by decreasing hepatic glucose production and intestinal absorption of glucose, and improving insulin sensitivity. It is indicated for the adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM) when treatment with both empagliflozin and metformin is appropriate. Synjardy® XR is not recommended for patients with type 1 DM or for the treatment of diabetic ketoacidosis. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 DM and established cardiovascular disease. However, the effectiveness of Synjardy® XR on reducing the risk of cardiovascular death in adults with type 2 diabetes mellitus and cardiovascular disease has not been established. The starting dose of Synjardy® XR should be individualized and based on the current regimen. Renal function should be assessed prior to starting Synjardy® XR therapy, as well as periodically thereafter. Dose adjustments are not required if eGFR is ≥45ml/min/1.73m Synjardy® XR should be avoided in patients with clinical or laboratory evidence of hepatic disease. There is evolving data regarding SGLT2 inhibitors and cardiovascular disease that may better define a role for these agents. A 2015 study by Zinman et al[3] published in the *NEJM* suggested that those treated with empagliflozin had a significantly lower rate of the primary composite outcome of death from cardiovascular causes, non-fatal MI, or non-fatal stroke when added to standard care as compared to placebo. The primary outcome occurred in 10.5% in the pooled empagliflozin group (both doses) vs 12.1% in the placebo

group (hazard ratio 0.86; p=0.04 for superiority). This study included patients with type 2 DM at high risk for cardiovascular events.

Recommendation: Synjardy® XR be non-preferred.

Clinical Criteria: Synjardy® XR is not recommended for patients with type 1 DM or for the treatment of diabetic ketoacidosis.

Board Decision: The Board unanimously approved all the above recommendation.

Trulance® (plecanatide); **PDL category**- GI,Misc

Plecanatide, the active ingredient of Trulance®, is a guanylate cyclase-C (GC-C) agonist. Both plecanatide and its active metabolite bind to GC-C and act locally on the luminal surface of the intestinal epithelium. Activation of GC-C results in an increase in both intracellular and extracellular concentrations of cyclic guanosine monophosphate (cGMP). Increases in intracellular cGMP stimulates secretion of chloride and bicarbonate into the intestinal lumen, mainly through activation of the cystic fibrosis transmembrane conductance regulator (CFRT) ion channel, which results in increased intestinal fluid and accelerated transit. It is indicated for adults for the treatment of chronic idiopathic constipation (CIC). The safety and efficacy of Trulance® were established in two double-blind, placebo-controlled, randomized, multicenter studies that included adult patients (N=1775) with symptoms of CIC. It was found to be significantly effective as compared with placebo for the primary endpoint of meeting criteria for being a responder to treatment. Comparator trials with other active ingredients were not noted.

Recommendation: Trulances® be non-preferred.

Clinical Criteria: For the treatment of chronic idiopathic constipation (CIC). Trulance is contraindicated in pediatric patients less than 6 years of age, and use should be avoided in pediatric patients 6 years to less than 18 years of age.

Board Decision: The Board unanimously approved all the above recommendation.

Utibron® Neohaler (indacaterol & glycopyrrolate powder); **PDL category**- Antiasthmatic- Adrenergic Anticholinergics

Utibron® Neohaler is a combination product containing the active ingredients of indacaterol (a long-acting beta2-adrenergic agonist; LABA) and glycopyrrolate (a long-acting muscarinic antagonist (LAMA), often referred to as an anticholinergic). Indacaterol acts locally in the lung at the beta2 receptors in bronchial smooth muscle, working as a bronchodilator. In the airways, glycopyrrolate exerts its effect through inhibition of muscarinic receptor M3 at the smooth muscle, which leads to bronchodilation. As do all LABA-containing products, Utibron® Neohaler has a box warning regarding the increased risk of asthma-related death. It is indicated as a combination product for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Utibron® Neohaler is *NOT* indicated for the relief of acute bronchospasm or for the treatment of asthma. There is evidence that Utibron® Neohaler is more effective as compared to both its individual components used as monotherapy (indacaterol and glycopyrrolate), and there is some evidence to support that Utibron® Neohaler is more effective than some other available combination products. However, it is recommended that Utibron® Neohaler

remain non-preferred and require prior authorization and be available to those who are unable to achieve therapeutic goals or who have failed on preferred, more cost effective alternatives.

Recommendation: Utibron® be non-preferred.

Clinical Criteria: Dosing limits apply, please see dosing consolidation list. DDI: Avoid concomitant use of Bevespi and Utibron with other anticholinergic-containing drugs, due to an increased risk of anticholinergic adverse events. Bevespi and Utibron should be used with extreme caution in patients being treated with MAO inhibitors, TCAs, or other drugs known to prolong the QTc interval.

Board Decision: The Board unanimously approved all the above recommendation.

Xadago® (safinamide mesylate); **PDL category**- Parkinsons-MAOIs

Safinamide, the active ingredient of Xadago®, is a monoamine oxidase B (MAO-B) inhibitor. While its exact mechanism of action for its effect in Parkinson's disease is not known, inhibition of MAO-B activity, by blocking the metabolism of dopamine, is thought to result in an increases in dopamine levels and a subsequent increase in dopaminergic activity in the brain. It is indicated for adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing 'off' episodes. It has not been shown to be effective as monotherapy for the treatment of PD. It does have contraindications with numerous different drugs and is also contraindicated in severe hepatic impairment. Xadago® was found to be significantly effective as compared with placebo for changing the mean total daily 'on' time, although the absolute changes in these times was small.

Recommendation: Xadago® be non-preferred in the new PDl category Parkinsons- MAOIs.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved all the above recommendation.

Xermelo® (telotristat ethyl); **PDL category**- GI- Misc.

Xermelo® contains telotristat ethyl as telotristat etiprate. Telotristat etiprate is the hippurate salt of telotristat ethyl. Telotristat, the active metabolite of telotristat ethyl, is an inhibitor of tryptophan hydroxylase, which mediates the rate limiting step in serotonin biosynthesis. Serotonin plays a role in mediating secretion, motility, inflammation, and sensation of the gastrointestinal tract, and it is over-produced in patients with carcinoid syndrome. By reducing the production of peripheral serotonin, it reduces the frequency of carcinoid syndrome diarrhea. It is indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy. Recommended dosage is to take 250mg TID with food. When short-acting octreotide is used in combination with Xermelo®, use octreotide at least 30 minutes after administering Xermelo®. Xermelo® treatment should be discontinued if severe constipation develops.

In clinical trials it was not demonstrated to be effective for other symptoms of carcinoid syndrome, such as abdominal pain or flushing. In a clinical trial compared with placebo, Xermelo® was found to significantly reduced daily bowel movements from baseline to 12 weeks.

Recommendation: Xermelo® be non-preferred.

Clinical Criteria: For the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

Board Decision: The Board unanimously approved all the above recommendation.

Xultophy® (insulin degludec & liraglutide); **PDL category**- Incretin Minmetics

Xultophy® is a combination product containing insulin degludec and liraglutide. Liraglutide is an analog of human glucagon-like peptide-1 (GLP-1) and acts as a GLP-1 receptor agonist, which increases glucose-dependent insulin release, decreases glucagon secretion, and slows gastric emptying. Insulin degludec is a long-acting basal human insulin analog that regulates glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM) inadequately controlled on basal insulin (<50U daily) or liraglutide (≤1.8mg daily). Xultophy® has not been studied in combination with prandial insulin and is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise due to the uncertain relevance of the rodent C-cell tumor findings in humans. It is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Xultophy® has not been studied in patients with a history of pancreatitis.

Recommendation: Xultophy® be non-preferred.

Clinical Criteria: At least two preferred drugs in this category must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved all the above recommendation.

Zejula® (niraparib); **PDL category**-Cancer

Niraparib, the active ingredient of Zejula®, is an inhibitor of poly(ADP-ribose) polymerase (PARP) enzymes, including PARP-1 and PARP-2, which play a role in DNA repair. In vitro studies have demonstrated that niraparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes, resulting in DNA damage, apoptosis, and cell death. It is indicated for the maintenance treatment of adults with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Recommended dosage is to take 300mg PO QD continuing until disease progression or unacceptable toxicity. Start treatment no later than 8 weeks after the most recent platinum-containing regimen. Bedtime administration may be a potential method for managing nausea. The safety and efficacy of Zejula® were assessed in a double-blind, placebo-controlled study that included patients with platinum-

sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer (N=553) who had received at least 2 prior platinum-containing regimens and were in response (complete or partial) to their most recent platinum-based regimen.

Recommendation: Zejula® be non-preferred.

Clinical Criteria: PA required to confirm appropriate diagnosis and testing.

Board Decision: The Board unanimously approved all the above recommendation.

FDA SAFETY ALERTS

General Anesthetic and Sedation Drugs: Drug Safety Communication - New Warnings for Young Children and Pregnant Women
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm533195.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA approves Jardiance to reduce cardiovascular death in adults with type 2 diabetes
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm531517.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Releases Draft Guidance for Industry: "Considerations in Demonstrating Interchangeability With a Reference Product."-Drug Information Update
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537135.pdf?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA confirms elevated levels of belladonna in certain homeopathic teething products
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm538684.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Chlorhexidine Gluconate: Drug Safety Communication - Rare But Serious Allergic Reactions
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm539575.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **September 12, 2017** 5:30pm –8:30pm at the Augusta Armory.